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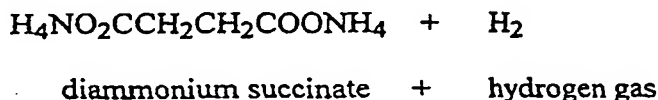
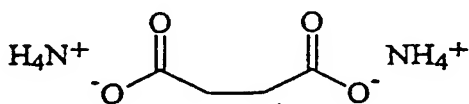
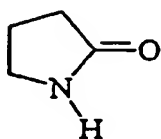
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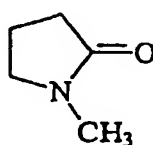
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(54) Title: METHODS OF MAKING PYRROLIDONES

catalyst / CH₃OH; catalyst = Pd/ZrO₂/C

2-pyrrolidone

+



N-methylpyrrolidone

(57) Abstract: The present invention provides methods for making N-methylpyrrolidine and analogous compounds via hydrogenation. Novel catalysts for this process, and novel conditions/yields are also described. Other process improvements may include extraction and hydrolysis steps. Some preferred reactions take place in the aqueous phase. Starting materials for making N-methylpyrrolidine may include succinic acid, N-methylsuccinimide, and their analogs.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

METHODS OF MAKING PYRROLIDONES

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STATEMENT OF GOVERNMENT RIGHTS

This invention was made with Government support under contract DE-AC0676RLO 1830 awarded by the U.S. Department of Energy. The Government has certain rights in this invention.

10

FIELD OF THE INVENTION

The present invention relates to methods of making pyrrolidones, especially N-methyl pyrrolidone ("NMP"), by hydrogenation.

15

BACKGROUND OF THE INVENTION

Olsen, in U.S. Patent No. 4,841,069 described reactions of succinic anhydride, methanol and hydrogen. In Example 1, Olsen described a reaction in which 67 g of succinic anhydride, 62 g of methanol, and 12.53 g of ammonia were heated 5 hrs in an autoclave at 300 °C with stirring. Olsen reported that 100% of the succinic anhydride was converted with a selectivity to N-methylsuccinimide ("NMS") of 90%. In Example 11, Olsen described a reaction in which 65 g of succinic anhydride, 41 g of methanol, and 12.15 g of ammonia, 12 g of 5% palladium on carbon catalyst, and 700 psig of hydrogen were heated 21 hrs at 290 °C with stirring. Olsen reported that 100% of the succinic anhydride was converted with a 60% selectivity to N-methylsuccinimide and a 30% selectivity to N-methylpyrrolidone.

Olsen, in U.S. Patent No. 4,814,464 (which is very similar to U.S. Patent No. 4,841,069), described the same or similar ammonolysis-alkylation reactions in which a succinic derivative such as the anhydride, acid or diester is reacted with ammonia and a C₁ to C₄ alkanol and converted to an N-alkylsuccinimide. Olsen stated that "In general, the reactants, substrate, ammonia, and alkanol, are used in about stiochiometric proportions. Too little ammonia or alkanol results in incomplete conversion, and too much ammonia is wasteful and produces undesirable by-products." However, Olsen also

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states that "preferably excess of the alcohol is used." It is reported that products can be separated by distillation or crystallization. See Col. 3, lines 50-59.

Olsen also remarked that the N-alkylsuccinimide can be reduced catalytically with hydrogen either continuously or batchwise. In Example 1, Olsen reported
5 hydrogenating NMS at 230 C for 2 hours over a nickel catalyst to yield a 60% NMS conversion with an 89% selectivity to NMP. In Example 3, Olsen reported reacting 73g dimethylsuccinate, 37g ammonium hydroxide, 12g of 5% palladium on carbon catalyst, and 700 psig of hydrogen for 21 hrs at 290 C with stirring. Olsen reported that 100% of the dimethylsuccinate was converted with a 70% selectivity to N-methylsuccinimide and
10 a 20% selectivity to N-methylpyrrolidone.

Koehler et al., in U.S. Patent No. 5,101,045, described a process for the preparation of N-substituted pyrrolidones by catalytic hydrogenation of maleic anhydride, maleic acid and/or fumaric acid in the presence of ammonia, a primary alcohol and a modified cobalt oxide catalyst. In Example 3, Koehler et al. stated that 75
15 ml of a 45% aqueous diammonium maleate solution and 75 ml methanol were hydrogenated for 42 hours at 230 C in the presence of 10 g of a modified cobalt oxide catalyst. Koehler et al. reported that the product contained 89 mol % NMP, 5.0 mol % pyrrolidine and methylpyrrolidine, and 2.7 mol % of succinimide and methylsuccinimide.

20 Liao, in U.S. Patent No. 3,092,638, and Hollstein et al., in U.S. Patent no. 3,681,387, described hydrogenating succinimide. Hollstein et al. run the hydrogenation in water over a palladium on carbon catalyst.

Liao, in U.S. Patent No. 3,080,377, Himmele et al., in U.S. Patent No. 3,198,808, Hollstein et al., in U.S. Patent no. 3,681,387, and Pesa et al. in U.S. Patent No. 4,263,175
25 described hydrogenating succinic acid or succinic anhydride in the presence of ammonia to yield 2-pyrrolidone. Catalysts used include: palladium on carbon, ruthenium on carbon, ruthenium on alumina, and cobalt oxide. Himmele et al. stated that an ammonium salt can be used in place of ammonia.

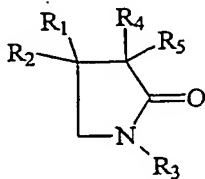
Chichery et al., in U.S. Patent No. 3,448,118, and Weyer et al. in U.S. Patents
30 Nos. 5,157,127 and 5,434,273, disclosed methods of making N-substituted pyrrolidones in which succinic anhydride, succinic acid, or the like is hydrogenated in the presence of a primary amine. Chichery et al. run their hydrogenations in water with a palladium on charcoal catalyst. Weyer et al. used a modified cobalt oxide catalyst.

zur Hausen et al., in U.S. Patent No. 4,780,547, described hydrogenation of NMS over a nickel catalyst. In Example 2, zur Hausen et al. stated that comparable results can be obtained using succinic anhydride and methylamine in place of NMS.

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SUMMARY OF THE INVENTION

The invention provides methods of making a compound having the formula:

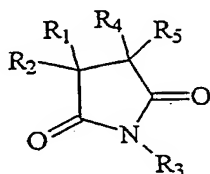


(C)

wherein R_1 , R_2 , R_4 , and R_5 are, independently, H or a C_1 to C_6 alkyl or substituted alkyl; and R_3 is H or a C_1 to C_6 alkyl or substituted alkyl. These methods involve hydrogenation.

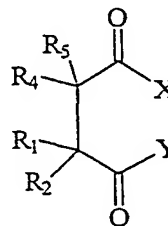
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In a first aspect, a composition containing a compound having the formula:



(A)

or



(B)

wherein R_1 , R_2 , R_4 , and R_5 are, independently, H or a C_1 to C_6 alkyl or substituted alkyl; or wherein R_2 and R_4 together are replaced by a double bond; R_3 is H or a C_1 to C_6 alkyl or substituted alkyl; and X and Y are, independently, OH, O^- , or where X and Y together are a bridging oxo; is reacted with hydrogen, in the presence of water and a catalyst. Preferably, the catalyst includes carbon, metal oxide and at least one metal selected from Pd, Rh, Pt, Ru, Ni or Co. In some embodiments, a compound of formula (A) is purified prior to hydrogenation. Thus, in some embodiments, a compound of formula (C) is made in a process having at least 3 steps. In a first step, a compound of formula (B) is reacted with an ammonia source, in the presence of water, to form a compound having formula (A). Then, in a second step, the compound of formula (A) is extracted into an organic solvent. In a third step, the compound of formula (A), that was extracted in the second step, is hydrogenated in the presence of a catalyst.

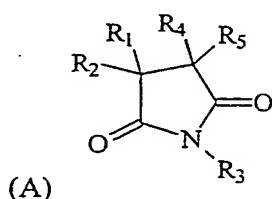
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It has also been surprisingly discovered that, in some processes, the yields of compound (C) can be increased substantially by hydrolyzing compositions formed during hydrogenation reactions of compounds (A) and/or (B). A portion of the composition formed by hydrogenating (A) and/or (B) can be hydrolyzed (i.e., reacted with water) to produce a compound or compounds of formula (C); this portion is referred to as a compound (C) precursor. To prevent over-reduction (and lower yields), the compound (C) precursor is separated from hydrogen, the hydrogenation catalyst, or both hydrogen and the catalyst.

In another aspect, the invention provides a method of making a compound of formula (C), in which a composition including a compound having the formula:



wherein R_1 , R_2 , R_4 , and R_5 are, independently, H or a C_1 to C_6 alkyl or substituted alkyl; and R_3 is H or a C_1 to C_6 alkyl or substituted alkyl; is reacted with and hydrogen in the presence of a Pd, Rh, Pt, Ru, Ni or Co catalyst; at a temperature of less than 220°C and for a time of less than 10 hours. In this method, compound (C) is obtained in a yield of at least 80%.

Advantages of various embodiments of the present invention include: higher yields, better purity, more stable catalysts, lower reaction temperatures, shorter reaction times, and lower costs. Unexpectedly superior results were discovered under various conditions, including: using a metal oxide (such as zirconia) textured catalyst; hydrogenating a succinimide below 220°C for less than ten hours; and hydrogenating aqueous phase compositions having a relatively high concentration of compound (B).

For fermentation or other biologically-derived compositions, it is desirable to separate out proteins and other contaminants, prior to the hydrogenation to produce compound (C). For example, proteins in these compositions could poison a hydrogenation catalyst. Thus, there may be important advantages in separating out an imide, such as compound A, and hydrogenating the extracted imide. An extraction step prior to the formation of N-methylpyrrolidine can produce unexpectedly superior results, especially for biologically-derived starting materials.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 illustrates a one-step reaction of diammonium succinate to 2-pyrrolidone and
5 NMP.

Fig. 2 illustrates a two-step reaction of diammonium succinate or succinimide to NMP.

DESCRIPTION OF THE PREFERRED EMBODIMENT(S)

10 Reactants in the inventive process include the compounds (A) and (B) described above. Preferably, R_1 , R_2 , R_4 , and R_5 are H or a lower alkyl, preferably methyl, ethyl or propyl, more preferably R_1 , R_2 , R_4 , and R_5 are all H. X and Y can be the same or different and preferably are OH or O^- (such as in an ionic oxygen species such as O^-
15 $[NH_4]^+$). In some preferred embodiments, X and Y together are a single bridging oxygen an anhydride such as succinic anhydride. Typically, X and Y are in an equilibrium such as between OH and anhydride or between $O^- [NH_4]^+$ and $OH + NH_3$. R_3 is preferably H or a lower alkyl, preferably methyl, ethyl or propyl; most preferably, R_3 is methyl.

The reactants may come from a variety of sources. For example, succinic acid can
20 be produced *in situ* from hydrogenation of maleic acid. In some preferred embodiments, the reactant composition is derived from fermentation or other biological process and will typically be in an aqueous solution or mixture (also referred to as an aqueous composition or aqueous phase composition).

When it is desirable to convert a compound of formula B (which for the purposes
25 of this disclosure can be called a "succinate"), the reaction mixture must contain an ammonia source, most typically ammonia or ammonium. The ammonia source can be added, such as by adding gaseous or aqueous ammonia, or can be present in the succinate feedstock, such as aqueous diammonium succinate. Preferably, ammonia (including ammonium) is present in a range of 1 to 3 molar ratio of ammonia to succinate, more
30 preferably 1 to 2. Ammonia can be present in the feedstock or added before or during the reaction. The succinate is preferably in aqueous solution, preferably having a concentration of 5 to 60 weight %, more preferably 15 to 30 wt. %. The reaction mixture preferably contains an alcohol, R_3OH where R_3 is a C_1 to C_6 alkyl or substituted alkyl, preferably methanol. The alcohol may be formed *in situ*, but is preferably added to the

reaction mixture as an alcohol. It has been found that the reaction is sensitive to alcohol content, with higher alcohol content leading to higher yields of the N-alkylated product such as NMP. Preferably, the alcohol is present in a ratio (alcohol : compound B) of at least about 2:1. The reaction preferably occurs in water.

5 The reactant (A) can be hydrogenated in solution or neat. In preferred embodiments, the reactant (A) is obtained from compound (B) and purified before hydrogenation. In many cases, the purified compound (A) may convert to product in greater yield and with fewer side products than an unpurified mixture. Most preferably, (A) is N-methyl-succinimide (NMS).

10 The product pyrrolidone, compound (C), preferably has the same $R_1 - R_5$ as in the reactant compound or compounds. In some preferred embodiments, the product is N-methyl pyrrolidone (NMP).

Formation of product (C) from compounds (A) or (B) requires hydrogenation over a hydrogenation catalyst. Preferably the catalyst contains Rh, Pd, Pt, Ru, Ni or Co
15 which are active metals for this hydrogenation. More preferably, catalyst also contains Re, such as in Pd-Re or Rh-Re. The hydrogenation catalyst typically includes a porous support material. Supports selected in the present invention are preferably selected to be stable in the reactor environment in which they are intended for use. Preferably, the supports are hydrothermally-stable, meaning that the support loses less than 15 % of its
20 surface area after 72 hours in water at 150 °C. More preferably, the support is hydrothermally-stable such that it loses less than 5 % of its surface area after 72 hours in water at 150 °C. Preferred support materials include porous carbon and rutile. An especially preferred support is a porous, high surface area activated carbon, such as carbons with CTC values around 120%, available from Calgon and Engelhard. For good
25 dispersion of the catalytic sites, the support preferably has a high surface area and a pore volume of 10 to 98%, more preferably 30 to 90%.

In preferred embodiments, a metal oxide is disposed on the porous support. Preferably, for aqueous phase applications, the oxide contains at least one of Zr, Ti, Hf, Ta, Nb, Mo, and W. Preferably, the metal oxide contains at least 50%, more preferably
30 at least 90%, by mass of an oxide or oxides of one or more of Zr, Ti, Hf, Ta, Nb, Mo, and W. In some embodiments, the metal oxide is substantially completely composed of an oxide or oxides of one or more of Zr, Ti, Hf, Mo, and W. The rutile form of titania is especially preferred. In alternative embodiments, oxides of other elements such as Si, Al,

Zn, Sn, V, Fe, U, Th, etc. may be used. The metal oxide is preferably present in 1 to 25 weight %, more preferably 5 to 10 weight percent of the total weight of the dried catalyst. Typically, the metal of the metal oxide is fully oxidized (for example TiO_2 , ZrO_2 , etc.) with terminal or bridging oxides; however, in less preferred embodiments the oxide
5 could contain, in addition to oxygen, hydrogen in hydroxyls (which may be difficult to differentiate from hydrated oxides), sulfides, cations, oxygen-containing anions, and the like. The catalyst metal (such as Pd, Rh, etc. including combinations of catalyst metals) is preferably present in 0.1 to 10 weight %, more preferably 2.5 to 5.0 weight percent of the total weight of the dried catalyst.

10 In some preferred embodiments, the catalyst is characterized by one or more of the following characteristics: a minimum, smallest dimension of at least about 100 μm , more preferably at least about 300 μm ; at least 70%, more preferably at least 80% of the catalyst component is within about 5 μm , more preferably about 2 μm , of 80% of the minimum area of the metal oxide. Preferably, at least about 5%, more preferably at least
15 about 10%, of the catalyst component, and at least about 5%, more preferably at least about 10%, of the metal oxide is disposed in pores that are at least about 10 μm , more preferably at least about 20 μm , away from the exterior of the support. The foregoing properties are conducted by cutting a catalyst particle or monolith to obtain a cross-section of at least about 100 μm in both height and width. The metal oxide is then
20 imaged by an elemental analysis spectroscopic technique, and the minimum area that encompasses 80% of the metal oxide is then identified. This area (or areas) is then increased by a 5 (or 2) μm margin around each area or areas. Then, the distribution of catalyst in the cross-sectional area is imaged by an elemental analysis spectroscopic technique; at least 70% of the catalyst component is within the area of the 80% of metal
25 oxide (including the margin). Amounts of each element is quantified by intensity. It is not necessary that all cross-sections exhibit the characteristics described herein, but, for a desired catalyst, at least some cross-section has these characteristics. Preferably, the 80% of the metal oxide plus 5 μm margin occupies less than 90%, more preferably less than 40%, of the total cross-sectional area. The converse preferably also occurs, that is, at
30 least 70%, more preferably at least 80%, of the metal oxide is within the minimum area of 80% of the catalyst component plus a 5 (or 2) μm margin around each area or areas.

Preferably, at least about 50% of the catalyst component is within about 10 μm of the exterior of the support. In some embodiments, some internal pores have at least 2 times, and in some cases at least 3 times, as much of the catalyst component as compared with the metal oxide. In preferred embodiments, the majority, more preferably at least
5 about 80%, of catalyst component, and/or the metal oxide, that is located within the interior of the support (that is, that portion of the catalyst component and/or metal oxide which is at least about 10 μm from the exterior of the support) is located in pores having at least one dimension of at least about 5 μm . The foregoing values are measured based on SEM analysis of cross-sections of catalysts.

10 Some preferred embodiments of the inventive catalysts may, alternatively, be described with reference to the method by which the catalyst is made. Alternatively, some preferred embodiments of the invention can be described by reactivities. For example, in some preferred embodiments, the catalyst exhibits a succinic acid conversion of at least 50% after 5 hours under the conditions set forth in Table 1.

15 Catalysts are preferably made by solution/colloid techniques. A porous support may be purchased or prepared by known methods. A metal oxide sol is prepared or obtained. A sol may be prepared, for example, by dissolving a metal compound and adding water or changing pH to form a sol. Each of the oligomeric or colloidal particles in the sol contain a metal and oxygen; these particles may also contain other components
20 such as halides, cations, etc. The sol could be prepared, for example, by dissolving a metal alkoxide, halide, etc. in an anhydrous solvent, then adding sufficient water to form a sol. In some preferred embodiments, organic solvents are avoided and the sol is prepared only in water. Conditions for preparing sols will depend on the type of metal and available ligands. In some preferred embodiments, the sol is prepared at between
25 about 10 and about 50 $^{\circ}\text{C}$. In some preferred embodiments, in aqueous solutions, the sol is preferably formed at a pH of between 1 and 6, more preferably between 2 and 5. The metal oxide precursor sol is contacted with the porous support. This could be done, for example, by dipping the support in the sol or colloid, or dispersing the sol in a volume of solvent equivalent to the incipient wetness of the support, so that the solvent exactly fills
30 the void fraction of the catalyst upon contacting and is dried to deposit the metal oxide on the surface of the support. In the case of a particulate support, such as activated carbon powders, the support and metal oxide precursor composition can be mixed in a suspension. The porous support is preferably not coated by a vapor-deposited layer, more

preferably the method of making the catalyst does not have any vapor deposition step. The catalyst component can be deposited subsequent to, or simultaneous with, the deposition of the metal oxide. The catalyst component can be impregnated into the support in a single-step, or by multi-step impregnation processes. In a preferred method, the precursor for the catalyst component is prepared in a sol that is deposited after, or codeposited with, the metal oxide precursor sol. In some preferred embodiments, the precursor for the catalyst component is prepared under the same conditions as the metal oxide precursor sol, for example as an aqueous colloidal mixture in the desired pH range. After the metal oxide and catalyst component have been deposited, the catalyst is typically dried. Also, following deposition, if desired, the catalyst component can be activated by an appropriate technique such as reduction under a hydrogen-containing atmosphere.

The inventive reactions can be accomplished in a one-step (A or B to C) or a two-step reaction (B to C). In some preferred embodiments, B is converted to A in a continuous process, and the resulting compound A is hydrogenated in a batch or continuous process. Preferably, A is purified prior to hydrogenation.

One example of a one-step reaction is illustrated in Fig. 1. A succinate, such as 20 weight % aqueous diammonium succinate, is hydrogenated in aqueous methanol at 265 °C and 1900 psi H₂ to produce 2-pyrrolidone (hereinafter referred to as "2-py," which is also known as 2-pyrrolidinone) and N-methylpyrrolidone. This route is conducted as a one step process; however, it has been found that the reaction proceeds through an N-methylsuccinimide intermediate. 2-py and NMP are obtained in a 90% yield based on the diammonium succinate starting material. The ratio NMP:2-py is about 2:1.

An example of a two-step reaction is illustrated in Fig. 2. In the first step of this route, a succinate, such as 20 weight % aqueous diammonium succinate or succinimide, is reacted with methanol at about 300 °C to produce N-methylsuccinimide. The first step does not require a catalyst. In the second step, aqueous N-methylsuccinimide is hydrogenated at 200 °C and 1900 psi H₂ for about 8 hours to produce NMP. The hydrogenation is conducted over a catalyst of Rh/ZrO₂/C or Rh-Re/C. Following hydrogenation, NMP can be isolated by distillation. If residues are present, the non-distilled residue is subjected to hydrolysis.

In some preferred embodiments, the succinimide produced in the first step is extracted into an organic solvent. Extraction solvents may include alkanes (such as

hexane), toluene, etc., and preferred extraction solvents include ethers and halocarbons. It has been found that chloroform is an excellent extraction solvent. Extractions can be conducted batchwise or in a continuous process.

For the one step reaction, temperature is preferably in the range of 200 to 350 °C, more preferably 230 to 280 °C. For the two-step reaction, better results are obtained if the second step is conducted at a lower temperature than the first step. The first step, which may be conducted in the absence of a catalyst, is preferably conducted at 250 to 350 °C, more preferably 280 to 320 °C. The second step, which requires a hydrogenation catalyst, has been found to yield better results if conducted at relatively low temperature, preferably at less than 230 °C, more preferably at 180 to 220 °C, and still more preferably 190 to 210 °C.

Another important variable is time. As is well-known, shorter reaction times are more economical and thus highly desirable. Preferably, reaction time for the one step process is less than about 24 hours, more preferably about 4 to about 10 hours. In the two-step process, reaction time for the first step is less than about 4 hours, more preferably less than about 0.5 hours. In some embodiments, time for the first step is about 0.2 to about 2.5 hours, preferably less than 1 hour. Reaction time for the second step is preferably less than about 24 hours, more preferably less than one hour, and in some embodiments about 10 minutes to about 10 hours, more preferably 10 to 30 minutes. In some preferred embodiments, the hydrogenation can be described as a function of time and mass of catalyst; preferably at least one half gram of reactant (preferably NMS) hour per gram catalyst, i.e., at least $(0.5 \text{ g reactant converted})(\text{h})/(\text{g catalyst})$. Alternatively, the hydrogenation preferably occurs at a rate of at least $(20 \text{ g reactant converted})(\text{h})/(\text{g catalyst metal})$.

Hydrogenation is preferably conducted at a pressure of 600-1800 psi, more preferably 1000-1400 psi.

The reactions can occur in any reactor suitable for use under the desired conditions of temperature, pressure, and solvent. Examples of suitable apparatus include: trickle bed, bubble column reactors, and continuous stirred tank.

It has been discovered that methods of the present invention can produce surprisingly high yields at selected conditions and reaction times. In preferred embodiments of the one step reaction, product C (preferably NMP) is obtained in a yield of at least 70%, more preferably at least 80%, in some preferred embodiments, NMP and

2-py are obtained in greater than 90% yield and an NMP/2-py ratio of at least 2.0. Yield of NMS is preferably at least 70% to about 90%, more preferably at least 80%. Conversion of NMS to NMP in methods of the present invention are preferably at least 70% to about 90%, more preferably at least 80%, with NMP/2-py ratio of at least 5, more preferably at least 50. Yields are measured by gas chromatography. The product can be purified by known procedures such as distillation or extraction.

In some preferred embodiments, at least a portion of the product composition obtained from a hydrogenation reaction is hydrolyzed and either recovered or recycled back into a reactor. The yield of pyrrolidones diminishes at long reaction times in the presence of hydrogen and a hydrogenation catalyst - this may be due to over-reduction of products. Therefore, the hydrolysis process is preferably conducted by removing the presence of either the hydrogen or the catalyst or both.

Hydrogenation of compounds (A) and/or (B) may result in a product composition containing compound (C) and a compound (C) precursor composition, where hydrolysis of the precursor composition yields additional compound (C). Following removal of hydrogen and/or hydrogenation catalyst, any portion of the product composition could be hydrolyzed. For example, the product composition could be hydrolyzed as a continuous stream. The hydrolysis reaction could also be accomplished, for example, by a packing the second half of a continuous flow reactor with an inert heat transfer packing so that following the conversion of an aqueous feedstock to a liquid product composition, the liquid composition could remain at hydrolysis reaction conditions outside of the presence of catalyst. Additionally, a secondary inert packed reactor could follow the primary reactor and gas/liquid separator to remove the hydrogen, and the secondary reactor could be operated at any desirable temperature and pressure combination that would result in the highest yield of product. Alternatively, compound (C) could be recovered, for example by distillation, from the product composition and the undistilled composition hydrolyzed to produce additional compound (C). Since higher yields of compound (C) precursor composition may result from lower temperature hydrogenation, in some embodiments, hydrogenation is conducted at below 200 °C, in some embodiments the hydrogenation is conducted in the range of 150-200 °C. The composition to be hydrolyzed preferably contains at least 20% by weight water, more preferably at least 50 wt. % water. Hydrolysis preferably is conducted at above 200 °C, in some embodiments,

in the range of 200-300 °C. In some embodiments, hydrolysis is conducted for 2 to 15 hours.

EXAMPLES

5 Catalyst Preparation Examples:

All catalysts prepared in the following examples were prepared on 20 X 50 mesh Engelhard 712A-5-1589-1 coconut shell carbon granules (nominal CTC number ~ 95%). Liquid holding capacity of the Engelhard carbon was determined to be ~ 0.76 cc/g (determined using the method of incipient wetness using D.I. 10 water). A commercially prepared $\text{Rh}(\text{NO}_3)_3$ solution (10.37% Rh by wt.) was used as the source of Rh for the Rh-containing catalyst.

5% Rh / C Catalyst

16.0071 g of the carbon granules were weighed into a 2 oz wide mouth glass jar, then the 15 jar containing the carbon was capped and set aside until needed. The liquid holding capacity of the 16.0071 g of carbon was calculated as 12.2 cc. The required wt. of Rh needed was calculated as follows:

$$[(16.0071 \text{ g C} \div 0.95) - 16.0071 \text{ g}] = 0.84 \text{ g Rh required}$$

The amount of the above $\text{Rh}(\text{NO}_3)_3$ solution was calculated as follows:

20 $0.84 \text{ g Rh needed} \div 0.1037 = 8.12 \text{ g of the } \text{Rh}(\text{NO}_3)_3 \text{ solution.}$

8.13 g of the $\text{Rh}(\text{NO}_3)_3$ solution (10.37% Rh by wt.) was weighed into an empty 25 ml graduated cylinder. Additional DI water was added so that the total solution volume was 12.2 ml (total solution wt. = 13.9635 g). The contents of the graduated cylinder were then well mixed to insure homogeneity. The 12.2 cc of the above prepared $\text{Rh}(\text{NO}_3)_3$ 25 solution was added dropwise (in ~ 0.8ml increments) to the 16.0071 g of carbon granules that had been previously weighed out. The jar was recapped following each ~ 0.8 ml addition of solution and shaken vigorously to insure uniform wetting of the carbon. After all of the solution had been added to the jar containing the carbon, the jar was allowed to stand for an additional ~30 minutes to allow the solution to completely soak 30 into the pores of the carbon. After standing for the ~ 30 minute period, the contents were again shaken vigorously to insure uniformity. The cap was then removed and placed in a vacuum oven to dry overnight (oven temperature = 100°C ; under house vacuum).

2.5% Rh / 2.5% Zr / C Catalyst

15.99 g of the carbon granules were weighed into a 2 oz wide mouth glass jar, then the jar containing the carbon was capped and set aside until needed.

$\text{ZrO}(\text{NO}_3)_2 \cdot x\text{H}_2\text{O}$ (anhydrous FW = 231.23 g / mole) was used as the source of Zr for this catalyst. 3.37 g of DI water and 0.41 g of 70% HNO_3 solution were added to a 25 ml graduated cylinder. Next, 1.0741 g of $\text{ZrO}(\text{NO}_3)_2 \cdot x\text{H}_2\text{O}$ was added to the graduate and the mixture heated on a hotplate until all of the $\text{ZrO}(\text{NO}_3)_2 \cdot x\text{H}_2\text{O}$ was dissolved. 4.09 g of the $\text{Rh}(\text{NO}_3)_3$ solution (10.37% Rh by wt.) was added to the graduate along with enough DI water to bring the total solution volume up to 12.2 cc. The contents of the graduated cylinder were then well mixed to insure homogeneity. The 12.2 cc of the above prepared Rh and Zr containing solution was added dropwise (in ~ 0.8ml increments) to the carbon granules that had been previously weighed out. The jar was recapped following each ~ 0.8 ml addition of solution and shaken vigorously to insure uniform wetting of the carbon. After all of the solution had been added to the jar containing the carbon, the jar was allowed to stand for an additional ~30 minutes to allow the solution to completely soak into the pores of the carbon. After standing for the ~30 minute period, the contents were again shaken vigorously to insure uniformity. The cap was then removed and placed in a vacuum oven to dry overnight (oven temperature = 100°C ; under house vacuum).

2.5% Rh / 2.5% Re / C Catalyst

16.00 g of the carbon granules were weighed into a 2 oz wide mouth glass jar. A commercially available perrhenic acid solution (54.5% Re by wt.) was used as the source of the Re for this catalyst. 0.778 g of perrhenic acid solution (54.5% Re by wt.) and 4.0666 g of $\text{Rh}(\text{NO}_3)_3$ solution (10.37% Rh by wt.) were weighed into a 25 ml graduated cylinder and enough DI water added to bring the total solution volume up to 12.2 cc. The 12.2 cc of Rh and Re containing solution was first well mixed to insure homogeneity, then added dropwise, in ~ 0.8 ml increments, to the jar containing the 16.00 g of carbon. The jar was recapped and shaken vigorously after each liquid addition. After all of the liquid had been added, the jar was allowed to stand capped for an additional 30 minutes to allow the liquid to soak into the pores of the carbon. After standing, the jar and its contents were again shaken vigorously to thoroughly mix the contents. The cap was then removed, and the open jar and its contents placed in a

vacuum oven to dry overnight (oven temperature = 100°C ; under house vacuum). The dried catalyst was loaded into the reaction chamber and reduced *in situ*.

Semi-Batch Reactor Run Examples:

Table 1 contains a summary of semi-batch reactor run results showing how the choice of catalyst, feedstock, and process conditions can affect reaction rates and product selectivities in the liquid phase synthesis of pyrrolidinones. The first 11 entries in the table are representative of hydrogenation reactions involving aqueous phase feedstocks. The entries in Table 2 are representative of hydrogenation reactions of feedstock materials performed in non-aqueous solvents. The description of the preparation of the feedstock solutions, the catalyst pretreatment process, and the semi-batch reactor run procedures are described below. Table 2 contains a summary of semi-batch reactor results showing how the choice of feedstock and process conditions can affect the reaction rates and product yields in the non-catalytic, hydrothermal synthesis of N-methylsuccinimide.

15 Preparation of Aqueous Feedstock Solutions Used in Semi-Batch Run Examples Aqueous Feedstock Solution #1

244.18 g (2.068 moles) of succinic acid was weighed into a ½ gallon poly bottle. Next, 583.76 g (32.400 moles) of DI water was also added to the bottle. The contents of the bottle were then gently agitated to try to break up lumps of solid succinic acid, and to try to wet all of the solid. Next, 239.17 g (4.142 moles NH₃ & 9.360 moles H₂O) of concentrated ammonia solution (29.5% NH₃ by wt.) was added to the slurried mixture in the bottle. The bottle, containing the succinic acid / ammonia mixture, was then recapped to prevent the loss of material. The capped bottle was again agitated to enhance the mixing of the reactants. The bottle warmed to ~ 50°C due to the neutralization reaction, and was cooled down to room temperature by holding the bottle under cold, running water for several minutes. All of the solid succinic acid, initially present, had dissolved and remained in solution after again reaching room temperature. Next, 133.07 g of methanol were added to the solution in the bottle, the bottle re-capped, and then shaken vigorously to thoroughly mix the resulting solution. The composition of the resulting solution was as follows:

Succinic Acid = 20.35% (by wt.)

NH₃ = 5.88% (by wt.)

Methanol = 11.09% (by wt.)

H₂O = 62.69% (by wt.)

The approximate molar ratio of this feedstock solution is approximately as follows:

$\text{NH}_3 / \text{Succinic Acid} / \text{Methanol} / \text{H}_2\text{O} = 2.0 / 1.0 / 2.0 / 20.2$

This feedstock solution was used in examples 1, 2, 3, & 5 in Table 1 and also in examples 1 & 2 in Table 2.

5 Aqueous Feedstock Solution #2

101.74 g (0.862 mole) of succinic acid was weighed into a 500 ml poly bottle along with 271.22 g (15.055 moles) of DI water. The mixture was gently agitated to break up the lumps of solid succinic acid, and to try to wet all of the solid. Next, 99.48 g of concentrated ammonia solution (29.5% NH_3 by wt.) (1.723 moles NH_3 + 3.893 moles H_2O) was added to the mixture in the bottle, the bottle re-capped, then shaken vigorously. After shaking, the bottle and its contents were cooled to room temperature. 27.60 g (0.861 mole) of methanol were added to the solution in the bottle, the bottle re-capped, then shaken to thoroughly mix the contents. The composition of the resulting solution was as follows:

15 Succinic Acid = 20.35% (by wt.)
 NH_3 = 5.87% (by wt.)
 Methanol = 5.52% (by wt.)
 H_2O = 68.27% (by wt.)

20 The approximate molar ratio of this feedstock solution was approximately as follows:

$\text{NH}_3 / \text{Succinic Acid} / \text{Methanol} / \text{H}_2\text{O} = 2.0 / 1.0 / 1.0 / 22.0$

This feedstock solution was used in example 4 in Table 1.

Aqueous Feedstock Solution #3

101.74 g (0.8615 mole) of succinic acid and 320.92 g (17.8138 moles) of DI water were weighed into a 500 ml poly bottle. The mixture was gently agitated to break up the lumps of solid succinic acid, and to try to wet all of the solid. Next, 49.74 g of concentrated ammonia solution (29.5% NH_3 by wt.) (0.861 moles NH_3 + 1.9465 moles H_2O) was added to the mixture in the bottle, the bottle re-capped, then shaken. After shaking, the bottle and its contents were cooled to room temperature. 27.60 g (0.861 mole) of methanol were then added to the solution in the bottle, the bottle re-capped, then shaken to thoroughly mix the contents. The composition of the resulting solution was as follows:

Succinic Acid = 20.35% (by wt.)
 NH_3 = 2.93% (by wt.)

Methanol = 5.52% (by wt.)

H₂O = 71.20% (by wt.)

The approximate molar ratio of this feedstock solution was approximately as follows:

NH₃ / Succinic Acid / Methanol / H₂O = 1.0 / 1.0 / 1.0 / 23.0

- 5 This feedstock solution was used in examples 6 & 7 in Table 1.

Aqueous Feedstock Solution # 4

- 68.22 g (0.6031 mole) of N-methylsuccinimide (NMS) and 281.78 g (15.64 moles) of DI water were weighed into a 500 ml poly bottle. The bottle was re-capped then shaken vigorously for several minutes until all of the NMS appeared to have dissolved. The composition of the resulting solution was as follows:

N-methylsuccinimide = 19.49% (by wt.)

H₂O = 80.51% (by wt.)

The approximate molar ratio of this feedstock solution is approximately as follows:

N-methylsuccinimide / H₂O = 1.0 / 25.9

- 15 This feedstock solution was used in examples 8, 9, 10 & 11 in Table 1.

Aqueous Feedstock Solution #5

- 85.37 g (0.8615 mole) of succinimide and 387.06 g (21.4852 moles) of DI water were weighed into a 500 ml poly bottle. Next, 27.60 g (0.8614 mole) of methanol was added to the mixture in the bottle, the bottle re-capped, then shaken vigorously. After shaking the bottle and its contents for ~ 15 minutes all but a small amount of the solid material appeared to have gone into solution (the amount of remaining undissolved solid material was probably less than ~ 0.2 g). The composition of the resulting solution was as follows:

Succinimide = 17.07% (by wt.)

25 Methanol = 5.52 % (by wt.)

H₂O = 77.41% (by wt.)

The approximate molar ratio of this feedstock solution was approximately as follows:

Succinimide / Methanol / H₂O = 1.0 / 1.0 / 24.9

This feedstock solution was used in example 3 in Table 2.

- 30 Aqueous Feedstock Solution #6

85.37 g (0.8615 mole) of succinimide, 359.42 g (19.9509 moles) of DI water, and 55.21 g (1.7232 mole) of methanol were weighed into a 500 ml poly bottle. The bottle was then capped and the contents shaken vigorously for ~ 10 minutes. Undissolved

material remained after that amount of time, so the capped bottle was held under hot running water for ~ 10 minutes (with occasional shaking). Even after holding under hot water for that amount of time, there still appeared to be ~ 0.1 g of undissolved white solid in the container. Upon cooling to room temperature, no additional white solid
5 material appeared to fall out of solution. The composition of the resulting solution was as follows:

Succinimide = 17.07% (by wt.)

Methanol = 11.04% (by wt.)

H₂O = 71.88% (by wt.)

10 The approximate molar ratio of this feedstock solution was approximately as follows:

Succinimide / Methanol / H₂O = 1.0 / 2.0 / 23.2

This feedstock solution was used in examples 4 & 5 in Table 2.

Aqueous Feedstock Solution #7

106.71 g (1.0769 mole) of succinimide and 324.33 g (18.0031 moles) of DI water
15 were weighed into a 500 ml poly bottle. The bottle was then capped and the contents shaken to dissolve the solid. It was necessary to heat up the contents of the bottle slightly by holding the bottle under hot running water. After heating the solution to ~ 37°C almost all of the solid had dissolved. The cap was removed and 69.09 g (2.156 moles) of methanol was added to the mixture. The bottle was again re-capped and
20 shaken to mix the contents, then allowed to cool to room temperature. A small amount of white solid fell out of solution upon cooling. Re-warming the solution (to ~ 40°C) was found to be sufficient to re-dissolve the solids. The composition of the resulting solution was as follows:

Succinimide = 21.34% (by wt.)

25 Methanol = 13.85% (by wt.)

H₂O = 64.85% (by wt.)

The approximate molar ratio of this feedstock solution is approximately as follows:

Succinimide / Methanol / H₂O = 1.0 / 2.0 / 16.7

This feedstock solution was used in example 6 in Table 2.

30 Description of the Semi-Batch Reactor System

Examples 1-11 of Table 1 and examples 1-6 of Table 2 were conducted in a modified 450 ml Parr autoclave system constructed of Hastelloy®C. The system incorporated a sealed magnetically driven stirrer assembly, internal cooling loop, internal

control thermocouple, 0-3000 psig pressure gauge, and filter-ended dip tube. The dip tube was used both for gas and liquid addition to the reactor vessel (but not simultaneously) and also for the removal of liquid product samples taken periodically during the runs. The reactor system was set up to run under a relatively fixed hydrogen or nitrogen pressure during the runs. This was accomplished by setting the gas cylinder delivery pressure to the desired run pressure (in advance of the run), then opening the vessel to the gas delivery system once the desired run temperature had been reached. The dip tube fitting had separate shutoff valves for the gas addition and liquid addition/removal. The shut off valve to the gas delivery system was closed prior to drawing out a liquid product sample. After sampling, the liquid shut off valve would be re-closed and the gas feed shutoff valve re-opened to the gas delivery system. A small change in the observed system pressure was usually encountered for the duration of the sampling period. The reactor vessel was electrically heated (Parr reactor heating jacket) and used a Parr temperature controller equipped with an integral tachometer and variable speed control. Times required for the initial heat up to run temperature were generally ~ ½ hour in duration.

Catalyst Pre-Treatment Procedures Used in Semi-Batch Reactor Run Examples (Pyrrolidinone Synthesis Runs)

Prior to use, all of the catalyst preparations described herein, were activated by an appropriate chemical reduction procedure. For all of the examples given in this document the catalyst activation procedure is accomplished via hydrogen reduction at an appropriate temperature condition. For all of the semi-batch run examples, the catalyst pretreatments (hydrogen reductions) were conducted in the semi-batch reactor vessel (450 cc Parr autoclave), prior to the addition of the liquid feedstock solution. All of the catalysts used in examples 1-11 in Table 1 were Rh-based catalysts prepared on the same carbon support material, and therefore all of the catalyst preps used in those examples received identical catalyst pre-treatments (H₂ reductions). In all cases, the weight of the dried, un-reduced catalyst preparation was nominally 3.75 g which was placed into a clean, dry reactor body. The rest of the reactor was then assembled and connected to the gas feed system, the cooling water lines, the rupture disc line, the control thermocouple connector, and to the stirrer drive motor. Following pressure testing, the reactor vessel was purged with N₂ or Argon to insure that all of the residual air was removed from the vessel prior to the addition of hydrogen. After purging with either N₂ or Argon, the

vessel is pressurized to 400 psig with whichever of the two inert gases were initially used. Next, 100 psig of additional hydrogen pressure is added to the reactor vessel and the vessel subsequently sealed off (reduction mixture was effectively a 20% H₂ in N₂ or Ar mixture). The internal stirrer is started and set at ~ 150 rpm to provide some internal
5 mixing of the gasses inside the reactor vessel. Once the stirrer started, the reactor vessel was heated to 120°C, where the temperature was maintained for a period of 4 hours. At the end of the 4 hours, the temperature controller was turned off, and the reactor vessel allowed to cool to room temperature. The spent reduction gasses were then vented from the reactor and the reactor again purged with N₂ or Argon.

10 Aqueous Feedstock Solution Addition and Procedure Used to Conduct Semi-Batch Reactor Run Examples (Pyrrolidinone Synthesis Runs)

The aqueous feedstock solution was added to the reactor vessel through the liquid addition/removal port on the reactor. Typically, ~ 150 cc of liquid feedstock solution was added to the reactor. After the liquid feedstock solution was added, the system was
15 initially purged with hydrogen gas to remove air that may have gotten into the reactor vessel during the liquid addition. The vessel was pressurized to ~ 500 psig with H₂, and the gas inlet line to the reactor vessel closed. The internal stirrer was turned on and adjusted to ~ 500 rpm, then the system was heated up to the desired run temperature. When the reactor vessel reaches the desired run temperature, a sample of the liquid
20 feedstock/product solution was removed from the reactor vessel, then the vessel was opened to the gas delivery system and the reactor pressure rose to the pre-set desired run pressure. The time when the reactor system was opened up to the gas delivery system is designated T = 0 hrs., or the time that the run is considered to have been started. Periodic liquid product samples were withdrawn from the reactor vessel and analyzed to monitor
25 the disappearance of starting materials and the formation of reaction products. Product samples are numbered according to how many hours had expired between the run start time and the time that a particular sample had been removed from the reactor. For instance, if the run start time for a particular reaction were 9:00 A.M. and a sample was withdrawn from the reactor at 10:30 A.M. (~ 1.5 hours after the run start time), then the
30 sample would be designated as the T + 1.5 hr. sample. The product samples were analyzed by gas chromatography and conversion and product selectivity data calculated for each catalyst and set of reaction conditions.

Description of NMS Synthesis Runs Conducted in the Semi-Batch Reactor System

Examples 1 – 6 of Table 2 were all examples of the non-catalyzed, hydrothermal synthesis of NMS from either diammonium succinate / methanol or succinimide / methanol mixtures. The reactions were conducted at elevated temperatures using a nitrogen cover gas. In these runs, the feedstock solution (~ 150 ml) was generally added to the reactor vessel following the usual pressure testing procedure. After the liquid had been added to the reactor vessel, the vessel was purged with nitrogen, to remove any air that may have gotten into the vessel during the liquid feedstock addition. Next, the reactor vessel was pressurized with additional nitrogen gas (typically 600-1000 psig depending upon the final run temperature) then closed off to the pressurized gas delivery system. The internal stirrer was turned on and adjusted to ~ 500 rpm, then the system was heated up to the desired run temperature (either 265°C or 300°C). A sample of the feed/product solution would be taken when the setpoint temperature was reached, then the reactor vessel would be opened up to the pressurized gas delivery system (pre-set to either 1900 or 2200 psig of N₂ pressure). Periodic liquid product samples were withdrawn from the reactor vessel and analyzed to monitor the disappearance of starting materials and the formation of reaction products. The product samples were analyzed by gas chromatography and conversion and product selectivity data calculated for each catalyst and set of reaction conditions. Table 1 contains a summary of semi-batch reactor run results showing how the choice of catalyst, feedstock, and process conditions can affect reaction rates and product selectivities in the liquid phase synthesis of pyrrolidinones.

Table 1: Synthesis of NMP – Semibatch Process Results

catalyst	Temp. (°C)	Pressure (MPa)	Feedstock solution	Time, (hr) at max. yield	% Conv.	Max. Yield of NMP+2-py (%)	NMP/2py mole ratio
5%Rh/C	265	13	1	21.0	98.5	83.3	1.58
2.5%Rh/2.5%Zr/C	265	13	1	21.3	97.5	95.2	2.31
2.5%Rh/2.5%Re/C	265	13	1	8.0	90.6	90.0	1.15
5%Rh/C	265	13	2	5.0	95.5	80.7	0.55
2.5%Rh/2.5%Re/C	200	13	1	24.0	93.5	47.2	0.21
5%Rh/C	265	13	3	7.0	89.6	70.9	0.86
2.5%Rh/2.5%Zr/C	200	13	3	23.5	80.4	24.8	0.16
5%Rh/C	265	13	4	8.0	95.6	74.1	2.15
2.5%Rh/2.5%Re/C	265	13	4	5.0	88.7	53.7	5.28
2.5%Rh/2.5%Zr/C	200	13	4	24.0	93.5	81.1	38.1
2.5%Rh/2.5%Re/C	200	13	4	8.0	94.8	88.8	67.3

All tests at 1900 psig (13.2 MPa)

As can be seen from the results in Table 1, increasing methanol increased the ratio of NMP. In a one-step reaction, better results may be obtained in a range of about 230 to 280 °C. Higher N-alkyl (e.g. NMP) yields are obtained at an alcohol:compound B ratio of at least 2. Surprisingly, we discovered that a metal oxide-containing catalyst resulted in superior results (see, for example, Example 2). Also, unexpectedly, by hydrogenating a succinimide in the presence of a Pd or Rh catalyst, at a temperature less than about 220 °C for less than 10 hours, we found that compounds (C), preferably NMP, can be obtained in a yield of at least 80%.

Table 2: Synthesis of NMS

Temp. (°C)	Pressure (MPa)	Feedstock Solution	Time, (hr) at max. yield	Max. Yield of NMS (%)	% conversion
265	13	1	3.0	66.9	100
300	13	1	3.5	83.3	100
265	13	5	4.0	43.2	75.3
300	13	6	2.5	82.3	97.8
300	15	6	3.0	79.0	99.1
300	13	7	0.5	87.5	89.0

As can be seen from Table 2, among other results, we discovered that surprisingly superior results are obtained from aqueous phase hydrogenations in which the molar ratio of compound (B):water is at least about 0.06, in some preferred embodiments in a range of 0.06 to 0.2.

Continuous Flow Reactor Run Examples:

Preparation of Aqueous Feedstock Solutions Used in Continuous Flow Reactor Run Examples

Aqueous Continuous Feedstock Solution #1

114.73 g (1.014 moles) of N-methylsuccinimide (Aldrich Chemical Co.) was weighed into a 1000 ml Erlenmeyer flask along with 474.01 g (26.312 moles) of deionized water. The contents of the flask were vigorously stirred until all of the soluble material had gone into solution. A small quantity (estimated to be less than 0.02 g) of black colored insoluble material remained suspended in the otherwise colorless solution. The black particles were removed by filtering. The composition of the resulting solution was as follows:

N-methylsuccinimide = 19.49% (by wt.)
 H₂O = 80.51% (by wt.)

The approximate molar ratio of this feedstock solution is approximately as follows:

N-methylsuccinimide / H₂O = 1.0 / 25.9

Aqueous Continuous Feedstock Solution #2

- 5 200.00 g (1.768 moles) of N-methylsuccinimide (Aldrich Chemical Co.) was weighed into a 32 oz Nalgene® poly bottle along with 826.18 g (45.861 moles) of DI water. The bottle was capped and shaken vigorously until all of the solid material had dissolved. The composition of the resulting solution was as follows:

N-methylsuccinimide = 19.49% (by wt.)

10 H₂O = 80.51% (by wt.)

The approximate molar ratio of this feedstock solution is approximately as follows:

N-methylsuccinimide / H₂O = 1.0 / 25.9

Description of the Continuous Flow Reactor System

- Examples 1-7 of Table 3 were generated in a small continuous flow reactor system configured as a trickle bed reactor. In this reactor configuration both gas and liquid feeds are introduced into the reactor in a co-current downflow manner. The reactor tube itself is an Autoclave Engineers 316 SS medium pressure reactor tube (0.750" O.D. X 0.098" wall thickness with coned and threaded ends). An internal thermowell tube (3/16" O.D. heavy walled 316 SS tube welded shut on one end) runs from the bottom end up through the entire heated length of the reactor tube, so that the reactor's temperature profile can be probed. The reactor tube is jacketed by a 2" diameter X 18" long heat exchanger through which hot oil is circulated to provide uniform heating of the reactor tube (catalyst is generally packed within the middle 14" of the 18" heated zone; bed temperatures can generally be maintained within +/- ~0.5°C). The oil was heated and circulated by a Julabo closed system heated pump. Liquid feeds were supplied to the reactor by an ISCO high-pressure syringe pump, equipped with a syringe heating jacket and heated liquid delivery lines. The liquid delivery line and gas delivery line entered the reactor together via an Autoclave Engineers "tee" at the top end of the reactor tube. Feed gases were metered into the reactor using Brooks high-pressure mass flow controllers. The gas feeds to the mass flow controllers were provided by a manifolded gas delivery system at constant pressure. A dome-loaded back-pressure regulator was used to maintain the reactor at the desired system pressure. Gaseous and liquid products are separated in chilled collection vessels; where liquid products were periodically drawn

off and analyzed. Gaseous materials were measured with a wet test meter, and gas samples were periodically withdrawn and analyzed by gas chromatography.

The catalyst used in the continuous flow reactor was made by an incipient wetness catalyst preparation technique. This was done by taking a 18.34g sample of an Engelhard carbon (CTC=95%, incipient wetness of 0.76 cc/g) to prepare a 2.5% rhodium
5 and 2.5% rhenium catalyst. The impregnation volume of this preparation was 13.9 ml. The amounts of rhodium and rhenium are specified as final weight percent of the reduced metal on the carbon support. Thus, the required weight of active metal precursor was back calculated to determine the necessary weight of rhodium nitrate and perrhenic acid.
10 For this example, 0.48g of rhodium metal was required, and thus 4.65 of rhodium nitrate stock solution was required (at 10.51% rhodium metal by weight). Also, 0.48g of rhenium metal was required, and thus 0.93g of perrhenic acid was required (at 52.09% rhenium metal by weight). 0.93 g of perrhenic acid and 4.67 g of rhodium nitrate was added to a graduated cylinder and stirred. The solution was then topped up to a final
15 volume of 14 ml, stirred, and allowed to stand for 5 minutes. The solution was then added in 1 to 2 ml aliquots to the jar containing the 18.34 g of carbon. After each addition, the jar was capped and shaken until the carbon flowed freely in the vessel. Upon addition of the entire volume of solution, the carbon was sticky and slightly clumped. The carbon sat closed at room temperature with intermittent agitation for 3
20 hours and appeared dry and mostly granular, with some material still adhering to the walls of the jar. The support was then placed uncapped in a vacuum oven set to 100 °C and 20 inHg house vacuum and left to dry overnight. The catalyst was reduced prior to use.

The reactor body was packed with about 10 ml of crushed quartz followed by 0.5
25 cm of quartz wool. The 2.5%Rh/2.5%Re on Engelhard 95%CTC carbon catalyst was added in 10 ml increments, followed by light tamping to achieve uniform packing. Upon addition of 40 ml (18.31g) of catalyst, the bed was capped with another 0.5cm of quartz wool. The reactor was then assembled in the flow reactor test stand. The catalyst was first
30 reduced at 120C for 16 hours under a cover gas of 4% hydrogen in argon at atmospheric pressure. Upon reduction, the cover gas was switched to hydrogen flowing at 18 SLPH and the pressure raised to 13 MPa while the column temperature was changed to the first operating point of 200 °C. After equilibrating the temperature and gas flowrate, the liquid feed was added via high pressure Isco liquid pump at 100 ml/hr. From previous

trickle bed experience, a total of 3 or more bed volumes of feed were allowed to pass through the reactor before it was considered equilibrated. Upon equilibration, approximately 20 to 30 ml of product was collected in a sample vial before the reactor conditions were adjusted and allowed to equilibrate again. During each sample period, a gas sample was taken from the low pressure side of the back pressure regulator and subjected to fixed gas analysis. The samples were immediately transferred to a refrigerator and batched for analysis on a GC. Prior to idling the reactor following a series of run conditions, approximately 3 bed volumes of deionized water was passed across the reactor, and the reactor was lowered to 100 °C and held at pressure under reducing conditions with a low flow of hydrogen until the next feed and series of run conditions. Results are shown in Table 3.

Table 3: Synthesis of NMP - Continuous Flow Reactor

Feedstock	1	1	1	2	2	2	2
H ₂ flow (slph)	18.2	18.2	14.4	8.3	8.3	18.2	18.2
H ₂ / NMS	4.3	4.3	4.6	4.2	4.2	4.6	4.6
psi	1900	1900	1900	1900	1900	1900	1200
Temp. (°C)	200	180	180	200	220	250	250
feed (ml/hr)	100	100	80	50	50	100	100
conversion %	93.6	78.0	85.3	98.7	99.4	97.8	88.2
NMP selec.	55.5	50.0	52.4	57.1	60.0	64.1	75.7
2-py selec.	0.7	0.0	0.0	1.1	1.8	0.0	0.6

Hydrolysis Examples

A composite testing feedstock was prepared by combining products obtained from the continuous flow testing (columns 2 and 3 of Table 3). The analysis of this composite is shown in the Table 4. 56.18 g of this material was loaded into a 300 ml Parr autoclave, sealed, and the purged repeatedly with nitrogen. The autoclave was stirred at 500 rpm, and a cover gas of nitrogen was used to pressurize the autoclave to 4 MPa. The reactor heater was turned on to a set point of 250 °C. After 30 minutes, the reactor achieved 250 °C and the pressure of nitrogen was increased to 9 MPa. The reactor was held at 250 °C and 9 MPa for 15.5 hours, after which it was quickly cooled and the

sample removed for analysis. The results are shown in the table below:

Table 4: Hydrolysis

	initial	final
% Succinimide	0.05	0.00
% N-Methylsuccinimide	3.09	2.98
% Methanol	0.15	0.13
% Gamma-Butyrolactone	0.15	0.04
% N-Methyl-2-Pyrrolidinone	6.42	10.42
% N-Butyl-2-Pyrrolidone	0.02	0.03
% 2-Pyrrolidinone	0.00	0.00

As can be seen from the Table, hydrolysis treatment substantially increased yield of the
5 desired product NMP.

A second hydrolysis experiment conducted for a shorter time (1.6 hr) with the
product obtained from the run in column 5 of Table 3 collected from the continuous
hydrogenation testing under the conditions of the first experiment showed no change in
the NMP yield. The difference in the results between the first and second experimental
10 runs was likely due to differences in hydrogenation conditions, although experimental
error is also a possibility. The feedstock for the second hydrolysis experiment was
obtained from a run at higher temperature and slower flow rate - conditions that may not
produce a compound (C) precursor compound.

15

CLOSURE

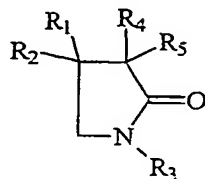
While preferred embodiments of the present invention have been described, it
will be apparent to those skilled in the art that many changes and modifications may be
made without departing from the invention in its broader aspects. The appended claims
20 are therefore intended to cover all such changes and modifications as fall within the true
spirit and scope of the invention.

CLAIMS

What is claimed:

1. A method of making a compound having the formula:

5

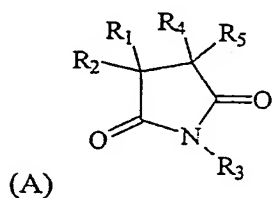


wherein R₁, R₂, R₄, and R₅ are, independently, H or a C₁ to C₆ alkyl or substituted alkyl;

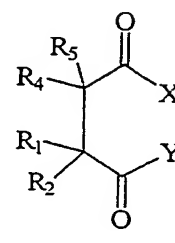
and R₃ is H or a C₁ to C₆ alkyl or substituted alkyl;

10

comprising reacting a composition comprising:
a compound having the formula:



or



wherein R₁, R₂, R₄, and R₅ are, independently, H or a C₁ to C₆ alkyl or substituted alkyl; or wherein R₂ and R₄ together are replaced by a double bond; R₃ is H or a C₁ to C₆ alkyl or substituted alkyl; and X and Y are, independently, OH, O⁻, or where X and Y together are a bridging oxo;

15

and hydrogen,

in the presence of water and a catalyst;

wherein the catalyst comprises carbon, metal oxide and at least one metal selected from the group consisting of Pd, Rh, Pt, Ru, Ni and Co.

20

2. The method of claim 1 comprising

a first step of reacting a compound of formula (B) with an ammonia source, in the presence of water, to form a compound of formula (A);

a second step of extracting the compound of formula (A) into an organic solvent;
and

a third step comprising hydrogenating the compound of formula (A), that was
extracted in the second step, in the presence of a catalyst.

5

3. The method of claim 1 wherein R₁, R₂, R₄, and R₅ are H.

4. The method of claim 3 wherein R₃ is H, methyl or ethyl.

10 5. The method of claim 4 comprising the step of reacting a compound of formula
(B) with an ammonia source; and

wherein the catalyst comprises Pd, Rh, or both Pd and Rh, and further wherein
the catalyst comprises Re.

15 6. The method of claim 3, wherein R₃ is C₁ to C₆ alkyl or substituted alkyl,
comprising the step of reacting a compound (B) with an ammonia source in a molar ratio
of ammonia:succinate of 1 to 3; and with alcohol in a molar ratio of alcohol:compound of
formula (B) of at least about 2:1.

20 7. The method of claim 4 wherein the metal oxide contains at least 90% by mass of
an oxide or oxides of one or more element selected from the group Zr, Ti, Hf, Ta, Nb,
Mo and W.

8. The method of claim 7 wherein the metal oxide is in 1 to 25 weight % of the total
25 weight of the catalyst.

9. The method of claim 8 wherein the catalyst metal comprises 0.1 to 10 weight
percent of the dried catalyst.

30 10. The method of claim 9, wherein hydrogen occurs in a reactor, further comprising
the step of purifying the compound of formula (C) by distillation which leaves an
undistilled residue; and

further comprising the step of hydrolyzing the residues to form hydrolyzed residues, and recycling the hydrolyzed residues back to the reactor.

11. The method of claim 3, wherein R_3 is methyl, wherein hydrogenation occurs in a reactor and produces a product composition comprising NMP;

further comprising a step of removing hydrogen or the catalyst from the product composition;

further comprising a step of removing at least a portion of the NMP from the product composition, leaving an NMP-depleted composition;

- 10 further comprising a step of hydrolyzing the NMP-depleted composition to produce a hydrolyzed composition; and

further comprising a step of either purifying NMP from the hydrolyzed composition or recycling the hydrolyzed composition to the reactor.

- 15 12. The method of claim 1 comprising a first step and a second step:

wherein R_3 is methyl or ethyl; wherein the first step comprises converting a compound of formula (B) into a compound of formula (A) in a temperature range of 250 to 350 °C in the presence of methanol or ethanol and an ammonia source;

- 20 wherein the second step comprises reacting a compound of formula (A) with hydrogen in the presence of the catalyst at a temperature of less than 230 °C, wherein the catalyst further comprises rhenium.

13. The method of claim 12 wherein R_3 is methyl, wherein R_1 , R_2 , R_4 , and R_5 are H; wherein the first step occurs in less than 1 hour;

- 25 wherein the second step occurs in less than 1 hour;

wherein NMP is obtained in a yield at least 70%, based on the initial amount of the compound of formula (B).

14. The method of claim 13 further comprising, subsequent to said second step, a hydrolysis step in the absence of hydrogen or the catalyst.

15. The method of claim 1 comprising the reaction of N-methyl succinimide and hydrogen;

in the presence of a catalyst comprising a metal selected from the group consisting of Pd, Rh, Pt, Ru, Ni and Co;

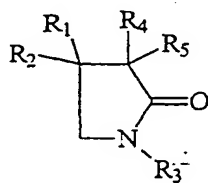
at a temperature of less than 220 °C and for a time of less than 10 hours;

wherein NMP is obtained in a yield of at least 80%, based on the initial amount of
5 N-methyl succinimide.

16. The method of claim 3 wherein R₃ is methyl; wherein R₁, R₂, R₄, and R₅ are H;
and

comprising obtaining a product mixture comprising a compound (C) precursor;
10 separating the compound (C) precursor from the catalyst, or from hydrogen, or
from both the catalyst and hydrogen, to form a separated compound (C) precursor; and
hydrolyzing the separated compound (C) precursor.

17. A method of making a compound having the formula:



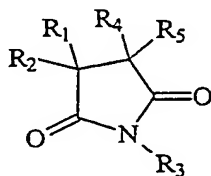
(C)

wherein R₁, R₂, R₄, and R₅ are, independently, H or a C₁ to C₆ alkyl or substituted
15 alkyl;

and R₃ is H or a C₁ to C₆ alkyl or substituted alkyl;

comprising reacting a composition comprising:

20 a compound having the formula:



(A)

wherein R₁, R₂, R₄, and R₅ are, independently, H or a C₁ to C₆ alkyl or substituted
alkyl; and R₃ is H or a C₁ to C₆ alkyl or substituted alkyl;

25 and hydrogen;

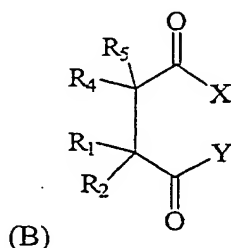
in the presence of a catalyst comprising a metal selected from the group consisting of Pd, Rh, Pt, Ru, Ni and Co;
 at a temperature of less than 220 °C and for a time of less than 10 hours;
 wherein compound (C) is obtained in a yield of at least 80%, based on the initial
 5 amount of (A).

18. The method of claim 17 wherein the composition comprises aqueous N-methyl succinimide.

10 19. The method of claim 17 wherein the catalyst comprises carbon, metal oxide and at least one metal selected from the group consisting of Pd, Rh, Pt, Ru, Ni and Co.

20. The method of claim 19 wherein the catalyst further comprises Re.

15 21. The method of claim 19 further comprising a step of reacting a compound of formula

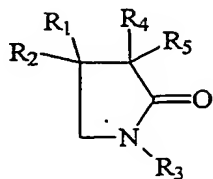


wherein R₁, R₂, R₄, and R₅ are H; or wherein R₂ and R₄ together are replaced by a double bond; R₃ is H or a C₁ to C₆ alkyl or substituted alkyl; and X and Y are,
 20 independently, OH, O⁻, or where X and Y together are a bridging oxo;
 with methanol and an ammonia source to form a compound of formula (A).

22. The method of claim 18 wherein the temperature is in the range of 180 to 220 °C.

25 23. The method of claim 22 wherein the step of hydrogenating aqueous N-methyl succinimide results in a product composition further comprising the steps of removing hydrogen or the catalyst from said product composition and, subsequently, hydrolyzing at least a portion of the product composition in the range of 200-300 °C.

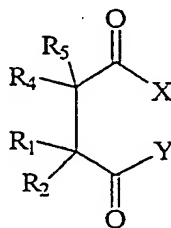
24. A method of making a compound having the formula:



5 wherein R₁, R₂, R₄, and R₅ are, independently, H or a C₁ to C₆ alkyl or substituted alkyl;

and R₃ is H or a C₁ to C₆ alkyl or substituted alkyl;

comprising a first step of reacting a composition comprising:
a compound having the formula:



10

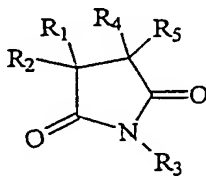
(B)

wherein R₁, R₂, R₄, and R₅ are, independently, H or a C₁ to C₆ alkyl or substituted alkyl; or wherein R₂ and R₄ together are replaced by a double bond; R₃ is H or a C₁ to C₆ alkyl or substituted alkyl; and X and Y are, independently, OH, O⁻, or where X and Y

15 together are a bridging oxo;

and an ammonia source,

in the presence of water, to form a compound having the formula:



(A)

20 wherein R₁, R₂, R₄, and R₅ are, independently, H or a C₁ to C₆ alkyl or substituted alkyl; or wherein R₂ and R₄ together are replaced by a double bond; R₃ is H or a C₁ to C₆ alkyl or substituted alkyl;

a second step of extracting the compound of formula (A) into an organic solvent;
and

a third step comprising hydrogenating the compound of formula (A), that was
extracted in the second step, in the presence of a catalyst.

5

25. The method of claim 24 wherein the compound of formula (B) is in a mixture
resulting from fermentation.

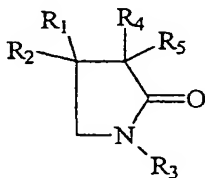
26. The method of claim 24 wherein the organic solvent is an ether or a halocarbon.

10

27. The method of claim 24 wherein the catalyst comprises carbon, metal oxide and
at least one metal selected from the group consisting of Pd, Rh, Pt, Ru, Ni and Co.

28. A method of making a compound having the formula:

15



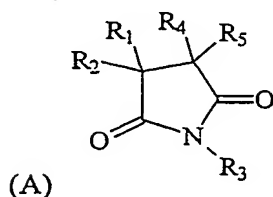
wherein R₁, R₂, R₄, and R₅ are, independently, H or a C₁ to C₆ alkyl or substituted
alkyl;

and R₃ is H or a C₁ to C₆ alkyl or substituted alkyl;

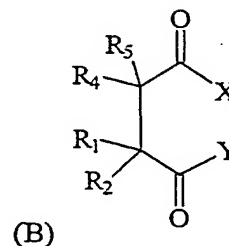
20

comprising reacting a composition comprising:

a compound having the formula:



or



wherein R₁, R₂, R₄, and R₅ are, independently, H or a C₁ to C₆ alkyl or substituted
alkyl; or wherein R₂ and R₄ together are replaced by a double bond; R₃ is H or a C₁ to C₆

alkyl or substituted alkyl; and X and Y are, independently, OH, O⁻, or where X and Y together are a bridging oxo;

and hydrogen,

in the presence of water and a catalyst;

5 to obtain a product mixture comprising a compound (C) precursor;

separating the compound (C) precursor from the catalyst, or from hydrogen, or from both the catalyst and hydrogen, to form a separated compound (C) precursor; and hydrolyzing the separated compound (C) precursor.

10 29. The method of claim 28 wherein the catalyst comprises carbon, metal oxide and at least one metal selected from the group consisting of Pd, Rh, Pt, Ru, Ni and Co.

30. The method of claim 28 wherein R₁, R₂, R₄, and R₅ are H, and R₃ is H, methyl or ethyl.

15

31. The method of claim 30 wherein the reaction with hydrogen is conducted at a temperature below 200 °C and the step of hydrolyzing the separated compound (C) precursor is conducted at a temperature above 200 °C.

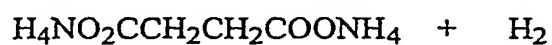
20 32. The method of claim 30 wherein the separated compound (C) precursor is in an aqueous solution comprising at least 20 weight % water.

33. The method of claim 32 wherein the reaction with hydrogen is conducted in a continuous flow reactor.

25

34. The method of claim 33 wherein the step of hydrolyzing the separated compound (C) precursor is conducted in a continuous flow reactor.

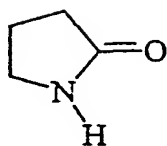
30 35. The method of claim 30 wherein compound (C) is recovered by distillation and the undistilled composition is hydrolyzed.



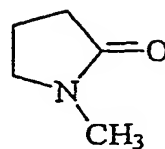
diammonium succinate + hydrogen gas



catalyst / CH₃OH; catalyst = Pd/ZrO₂/C



2-pyrrolidone



N-methylpyrrolidone

Fig. 1

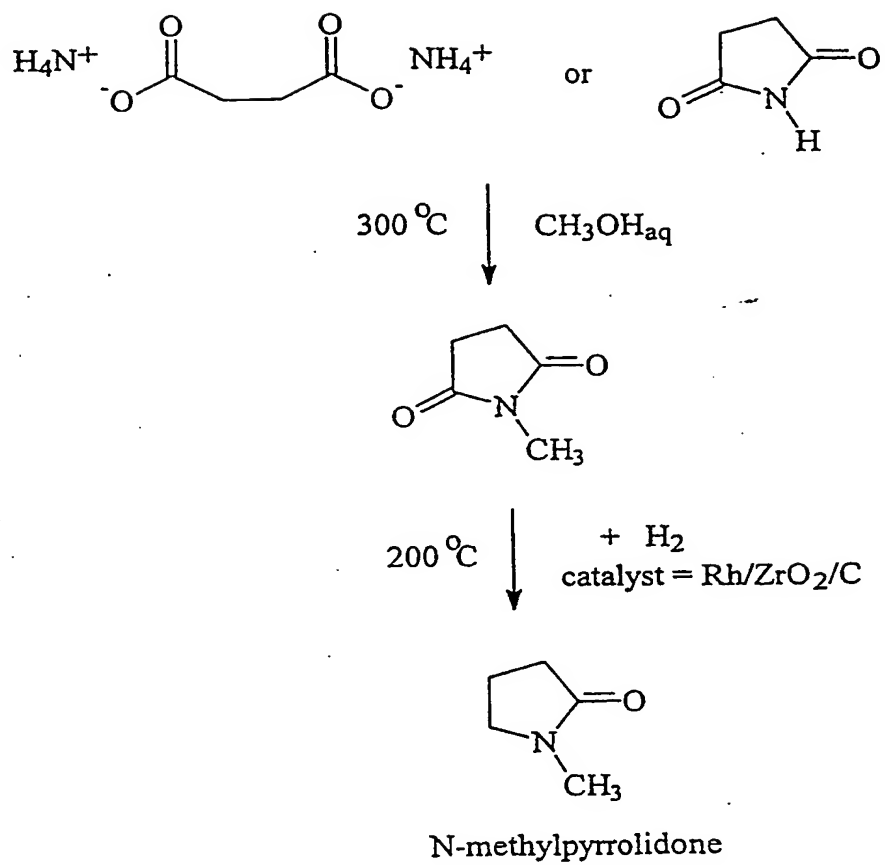


Fig. 2

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 02/19372

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D207/26

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 814 464 A (OLSEN ROBERT J) 21 March 1989 (1989-03-21) the whole document	1, 2, 17, 24
X	US 4 731 454 A (OTAKE MASAYUKI ET AL) 15 March 1988 (1988-03-15) the whole document	1, 2, 17, 24
	-/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

9 September 2002

Date of mailing of the international search report

24/10/2002

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
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Tel (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+31-70) 340-3016

Authorized officer

Frelon, D

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 02/19372

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE WPI Week 198811 Derwent Publications Ltd., London, GB; AN 1988-073882 XP002212826 & JP 63 027476 A (MITSUBISHI CHEM IND LDT), 5 February 1988 (1988-02-05) abstract -& PATENT ABSTRACTS OF JAPAN vol. 012, no. 237 (C-509), 6 July 1988 (1988-07-06) & JP 63 027476 A abstract -& DATABASE CHEMABS 'Online! chemical abstracts service, colombus, ohio, us; XP002212825 retrieved from STN Database accession no. 109:170226 abstract & JP 63 027476 A</p> <p style="text-align: center;">---</p>	1,2,17, 24
X	<p>EP 0 252 242 A (HUELS CHEMISCHE WERKE AG) 13 January 1988 (1988-01-13) the whole document</p> <p style="text-align: center;">---</p>	1,17
X	<p>US 4 851 546 A (GRAHAM ANNE M ET AL) 25 July 1989 (1989-07-25) the whole document</p> <p style="text-align: center;">---</p>	1,17
X	<p>US 3 092 638 A (LIAO HSIANG P ET AL) 4 June 1963 (1963-06-04) the whole document</p> <p style="text-align: center;">---</p>	1,17
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X	<p>US 3 198 808 A (WALTER HIMMELE ET AL) 3 August 1965 (1965-08-03) the whole document</p> <p style="text-align: center;">---</p>	1
X	<p>EP 0 027 022 A (STANDARD OIL CO OHIO) 15 April 1981 (1981-04-15) the whole document</p> <p style="text-align: center;">---</p>	1
	-/--	

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 02/19372

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 841 069 A (OLSEN ROBERT J) 20 June 1989 (1989-06-20) the whole document	1
X	EP 0 460 474 A (BASF AG) 11 December 1991 (1991-12-11) the whole document	1
X	EP 0 464 359 A (BASF AG) 8 January 1992 (1992-01-08) the whole document	1
X	US 4 904 804 A (MATSON MICHAEL S) 27 February 1990 (1990-02-27) the whole document	1
X	EP 0 745 589 A (BAYER AG) 4 December 1996 (1996-12-04) the whole document	1
X	EP 0 545 150 A (BASF AG) 9 June 1993 (1993-06-09) the whole document	1
X	US 3 080 377 A (LIAO HSIANG P) 5 March 1963 (1963-03-05) the whole document	2

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claim 28 and claims dependent thereon relate to an extremely large number of possible methods because of the term "a compound (C) precursor" which is nowhere specified. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT cannot be found. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to methods of preparation of compounds of formula (C) as defined in claim 1 and as supported in the description, page 3.

Present claims 17 and claims dependent thereon relate to methods defined by reference to a desirable characteristic or property, namely the NMP *obtention of a yield of at least 80%, based on the initial amount of NMS.* An attempt is made to define the methods by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
 PCT/US 02/19372

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6:4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 02/19372

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 02/19372

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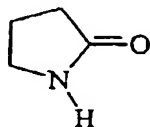
(54) Title: METHODS OF MAKING PYRROLIDONES



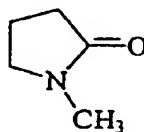
diammonium succinate + hydrogen gas



catalyst / CH₃OH; catalyst = Pd/ZrO₂/C



2-pyrrolidone



N-methylpyrrolidone

(57) Abstract: The present invention provides methods for making N-methylpyrrolidine and analogous compounds via hydrogenation. Novel catalysts for this process, and novel conditions/yields are also described. Other process improvements may include extraction and hydrolysis steps. Some preferred reactions take place in the aqueous phase. Starting materials for making N-methylpyrrolidine may include succinic acid, N-methylsuccinimide, and their analogs.

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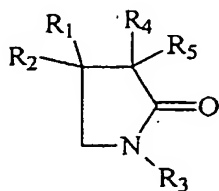
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

AMENDED CLAIMS

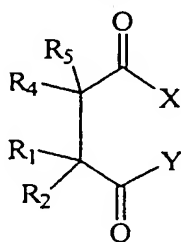
[received by the International Bureau on 24 December 2002 (24.12.02)
claim 1-35 replaced by claims 1-46];

1. A method of making a compound having the formula (C) below:



(C)

wherein R_1 , R_2 , R_4 , and R_5 are, independently, H or a C_1 to C_6 alkyl or substituted alkyl; and wherein R_3 is H or a C_1 to C_6 alkyl or substituted alkyl; the method comprising reacting a compound with an alcohol and hydrogen in the presence of water and a catalyst; the compound having the formula (B) below:

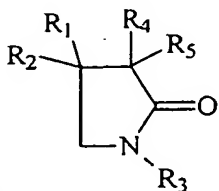


(B)

wherein R_1 , R_2 , R_4 , and R_5 are, independently, H or a C_1 to C_6 alkyl or substituted alkyl, or wherein R_2 and R_4 together are replaced by a double bond; R_3 is H or a C_1 to C_6 alkyl or substituted alkyl; and X and Y are, independently, OH, O⁻, or where X and Y together are a bridging oxo; and

wherein the catalyst comprises carbon, metal oxide and at least one metal selected from the group consisting of Pd, Rh, Pt, Ru, Ni and Co.

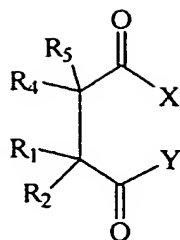
2. A method of producing a compound having formula (C) below:



(C)

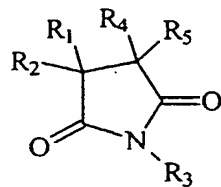
wherein R_1 , R_2 , R_4 , and R_5 are, independently, H or a C_1 to C_6 alkyl or substituted alkyl; and wherein R_3 is H or a C_1 to C_6 alkyl or substituted alkyl; the method comprising:

a first step of reacting a compound of formula (B)



(B)

with an ammonia source, in the presence of water, to form a compound of formula (A);



(A)

a second step of extracting the compound of formula (A) into an organic solvent; and
a third step comprising hydrogenating the compound of formula (A), that was extracted in the second step, in the presence of a catalyst.

3. The method of claim 1 wherein R_1 , R_2 , R_4 , and R_5 are H.
4. The method of claim 3 wherein R_3 is H, methyl or ethyl.
5. The method of claim 1 further comprising providing ammonia during the reacting, wherein the catalyst comprises Re and at least one of Pd and Rh.
6. The method of claim 1 comprising reacting the compound of formula (B) with an ammonia source in a molar ratio of ammonia:compound of formula (B) of 1 to 3; the alcohol being present in a molar ratio of alcohol:compound of formula (B) of at least about 2:1, wherein R_3 is C_1 to C_6 alkyl or substituted alkyl.
7. The method of claim 1 wherein the metal oxide contains at least 90% by mass of an oxide or oxides of one or more element selected from the group Zr, Ti, Hf, Ta, Nb, Mo and W.
8. The method of claim 7 wherein the metal oxide is 1 to 25 weight % of the total weight of the catalyst.

9. The method of claim 8 wherein the catalyst metal comprises from 0.1 to 10 weight percent of a dried form of the catalyst.

10. The method of claim 9, wherein hydrogen occurs in a reactor, and further comprising:

purifying the compound of formula (C) by distillation which leaves an undistilled residue;

hydrolyzing at least some of the residue to form hydrolyzed residue, and

recycling the hydrolyzed residue back to the reactor.

11. The method of claim 3, wherein R_3 is methyl, wherein hydrogenation occurs in a reactor and produces a product composition comprising N-methyl pyrrolidone (NMP); and further comprising:

removing at least one of hydrogen and the catalyst from the product composition;

removing at least a portion of the NMP from the product composition, leaving an NMP-depleted composition;

hydrolyzing the NMP-depleted composition to produce a hydrolyzed composition; and

a step comprising purifying NMP from the hydrolyzed composition or recycling the hydrolyzed composition to the reactor.

12. The method of claim 2 wherein the first step comprises a temperature range of 250 to 350 °C, wherein the third step comprises a temperature of less than 230 °C; wherein the catalyst comprises one or more metals selected from the group consisting of Re, Rh, Pd, Pt, Ru, Ni and Co, and wherein R_3 is methyl or ethyl.

13. The method of claim 12 wherein R_3 is methyl; wherein R_1 , R_2 , R_4 , and R_5 are H; wherein the first step occurs in less than 1 hour; wherein the third step occurs in less than 1 hour; and wherein N-methyl pyrrolidone is obtained in a yield at least 70%, based on the initial amount of the compound of formula (B).

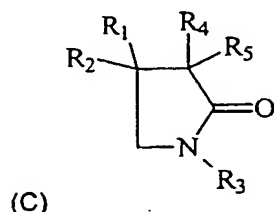
14. The method of claim 13 further comprising, subsequent to said third step, a hydrolysis step in the absence of at least one of hydrogen or the catalyst.

15. The method of claim 2 wherein compound of formula (A) is N-methyl succinimide and wherein the third step is conducted at a temperature of less than 220 °C and for a time of less than 10 hours; and wherein N-methyl pyrrolidone is obtained in a yield of at least 80%, based on the initial amount of N-methyl succinimide.

16. The method of claim 3 wherein R_3 is methyl; wherein R_1 , R_2 , R_4 , and R_5 are H; and further comprising:

obtaining a product mixture comprising a compound (C) precursor;
 separating the compound (C) precursor from the catalyst, or from hydrogen, or from both the catalyst and hydrogen, to form a separated compound (C) precursor; and
 hydrolyzing the separated compound (C) precursor.

17. A method of making a compound having the formula:

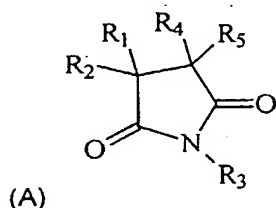


wherein R₁, R₂, R₄, and R₅ are, independently, H or a C₁ to C₆ alkyl or substituted alkyl;

and R₃ is H or a C₁ to C₆ alkyl or substituted alkyl;

comprising reacting a composition comprising:

a compound having the formula:



wherein R₁, R₂, R₄, and R₅ are, independently, H or a C₁ to C₆ alkyl or substituted alkyl; and R₃ is H or a C₁ to C₆ alkyl or substituted alkyl;

and hydrogen;

in the presence of a catalyst comprising a metal oxide and comprising from 0.1% to 10% catalytic metal by weight, the catalytic metal comprising a least one member selected from the group consisting of Pd, Rh, Pt, Ru, Ni and Co;

at a temperature of less than 220 °C and for a time of less than 10 hours;

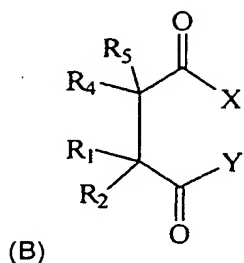
wherein compound (C) is obtained in a yield of at least 80%, based on the initial amount of (A).

18. The method of claim 17 wherein the composition comprises aqueous N-methyl succinimide.

19. The method of claim 17 wherein the catalyst comprises carbon.

20. The method of claim 19 wherein the catalyst further comprises Re.

21. The method of claim 19 further comprising a step of reacting a compound of formula

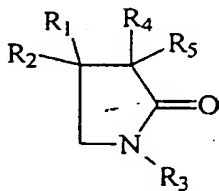


wherein R_1 , R_2 , R_4 , and R_5 are H; or wherein R_2 and R_4 together are replaced by a double bond; R_3 is H or a C_1 to C_6 alkyl or substituted alkyl; and X and Y are, independently, OH, O^- , or where X and Y together are a bridging oxo; with methanol and an ammonia source to form a compound of formula (A).

22. The method of claim 18 wherein the temperature is in the range of 180 to 220°C.

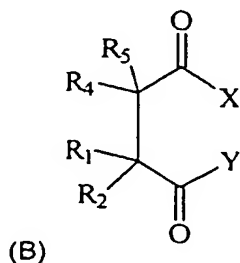
23. The method of claim 22 wherein the step of hydrogenating aqueous N-methyl succinimide results in a product composition further comprising the steps of removing hydrogen or the catalyst from said product composition and, subsequently, hydrolyzing at least a portion of the product composition in the range of 200-300°C.

24. A method of making a compound having the formula:



wherein R_1 , R_2 , R_4 , and R_5 are, independently, H or a C_1 to C_6 alkyl or substituted alkyl; and R_3 is H or a C_1 to C_6 alkyl or substituted alkyl;

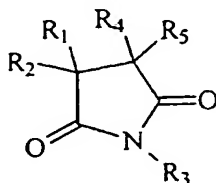
comprising a first step of reacting a composition comprising:
a compound having the formula:



wherein R_1 , R_2 , R_4 , and R_5 are, independently, H or a C_1 to C_6 alkyl or substituted alkyl; or wherein R_2 and R_4 together are replaced by a double bond; R_3 is H or a C_1 to C_6 alkyl or substituted alkyl; and X and Y are, independently, OH, O^- , or where X and Y together are a bridging oxo;

and an ammonia source,

in the presence of water, to form a compound having the formula:



(A)

wherein R_1 , R_2 , R_4 , and R_5 are, independently, H or a C_1 to C_6 alkyl or substituted alkyl; or wherein R_2 and R_4 together are replaced by a double bond; R_3 is H or a C_1 to C_6 alkyl or substituted alkyl;

a second step of extracting the compound of formula (A) into an organic solvent; and

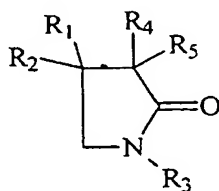
a third step comprising hydrogenating the compound of formula (A), that was extracted in the second step, in the presence of a catalyst.

25. The method of claim 24 wherein the compound of formula (B) is in a mixture resulting from fermentation.

26. The method of claim 24 wherein the organic solvent is an ether or a halocarbon.

27. The method of claim 24 wherein the catalyst comprises carbon, metal oxide and at least one metal selected from the group consisting of Pd, Rh, Pt, Ru, Ni and Co.

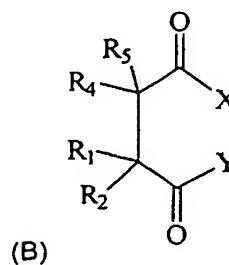
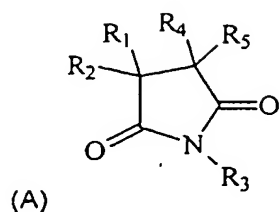
28. A method of making a compound having the formula (C) below:



(C)

wherein R_1 , R_2 , R_4 , and R_5 are, independently, H or a C_1 to C_6 alkyl or substituted alkyl; and R_3 is H or a C_1 to C_6 alkyl or substituted alkyl; the method comprising:

providing a composition comprising a compound having the formula (A) or (B) below:



wherein R_1 , R_2 , R_4 , and R_5 are, independently, H or a C_1 to C_6 alkyl or substituted alkyl; or wherein R_2 and R_4 together are replaced by a double bond; R_3 is H or a C_1 to C_6 alkyl or substituted alkyl; and X and Y are, independently, OH, O^- , or where X and Y together are a bridging oxo;

reacting the compound with hydrogen in the presence of water and a catalyst to obtain a product mixture comprising a compound (C) precursor;

separating the compound (C) precursor from the catalyst, or from hydrogen, or from both the catalyst and hydrogen, to form a separated compound (C) precursor; and

hydrolyzing the separated compound (C) precursor.

29. The method of claim 28 wherein the catalyst comprises carbon, metal oxide and at least one metal selected from the group consisting of Pd, Rh, Pt, Ru, Ni and Co.

30. The method of claim 28 wherein R_1 , R_2 , R_4 , and R_5 are H, and R_3 is H, methyl or ethyl.

31. The method of claim 30 wherein the reaction with hydrogen is conducted at a temperature below 200 °C and the step of hydrolyzing the separated compound (C) precursor is conducted at a temperature above 200 °C.

32. The method of claim 30 wherein the separated compound (C) precursor is in an aqueous solution comprising at least 20 weight % water.

33. The method of claim 32 wherein the reaction with hydrogen is conducted in a continuous flow reactor.

34. The method of claim 33 wherein the step of hydrolyzing the separated compound (C) precursor is conducted in a continuous flow reactor.

35. The method of claim 30 wherein compound (C) is recovered by distillation and the undistilled composition is hydrolyzed.

36. The method of claim 1 wherein the metal oxide comprises at least one metal selected from the group consisting of Zr, Hf, Ta, Nb, Mo, W, Zn, Sn, V, Fe, U and Th.

37. A method of producing N-methyl pyrrolidone comprising:
 providing a catalyst comprising a first metal, an oxide material comprising a second metal and a carbon support, the second metal comprising at least one member of the group consisting of Zr, Hf, Ta, Nb, Mo, W, Zn, Sn, V, Fe, U and Th;
 flowing an aqueous solution comprising succinimide over the catalyst in the presence of hydrogen to catalytically hydrogenate the succinimide, the hydrogenation forming N-methyl pyrrolidone and 2-pyrrolidone, a product ratio of N-methyl pyrrolidone to 2-pyrrolidone being greater than 5:1.

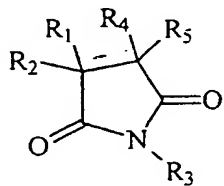
38. The method of claim 37 wherein the second metal further comprises a member of the group consisting of Si, Ti and Al.

39. The method of claim 37 wherein the first metal comprises Rh and the second metal comprises Zr.

40. The method of claim 37 wherein the catalyst contains from 0.1% to 10% of the first metal by weight.

41. The method of claim 37 wherein the catalyst comprises from 1% to 25% oxide material, by weight.

42. A method of forming a pyrrolidone compound comprising:
 forming a solution comprising an initial compound having the formula below:



providing the solution into a reactor containing a catalyst comprising a metal oxide, the metal oxide having at least one metal selected from the group consisting of Zr, Hf, Ta, Nb, Mo, W, Zn, Sn, V, Fe, U and Th;

flowing hydrogen into the reactor;

reacting the hydrogen with the initial compound in the presence of the catalyst, the reaction converting the initial compound into the pyrrolidone compound.

43. The method of claim 42 wherein the solution is an aqueous solution having a molar ratio of initial compound to water of about 1:25.9.

44. The method of claim 42 wherein the reactor is a continuous flow reactor and wherein the catalyst is a solid catalyst comprising a porous carbon support.
45. The method of claim 42 wherein R_3 is methyl.
46. The method of claim 42 wherein R_1 , R_2 , R_4 , and R_5 are all H.

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